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Article

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Enantio- and diastereoselective Nitro-Mannich Reaction of α-Aryl Nitromethanes with Amidosulfones catalyzed by phase-transfer catalysts

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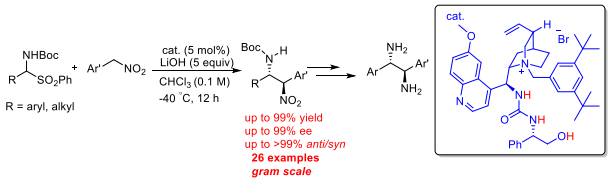
Supporting Information Placeholder



ABSTRACT: A high-yield, highly diastereo- and enantioselective nitro-Mannich reaction of α-aryl nitromethanes with amidosulfones catalyzed by a novel chiral phase-transfer catalyst, bearing multiple H-bonding donors, derived from quinine was developed. A variety of *α*-aryl nitromethanes and amidosulfones were investigated; and the corresponding products were obtained in excellent yields with excellent diastereo- and enantioselectivities (up to 99% yield, >99:1 dr and >99% ee). As a demonstration of synthetic utility, the resulting *β*-nitroamines could be converted to corresponding *meso*-symmetric and optically pure unsymmetric *anti*-1,2-diarylethylenediamines.

INTRODUCTION

Vicinal diamines are one of most important core structures of many drugs. Moreover, they are also used as chiral ligands and have been widely used in asymmetric catalysis.[1] As a result, chiral vicinal diamines have been the subject of research, and a number of highly stereoselective synthetic methodologies have been developed.[2] Among structurally diverse vicinal diamines, optically active 1,2-diarylethylenediamines have been widely used to prepare chiral ligands, organocatalysts and biologically active molecules.[3] Despite their utility, effective methods for the preparation of optically pure 1,2-diarylethylenediamines are still limited.[1b] Among these existing synthetic methodologies, cumbersome asymmetric synthesis started from chiral starting materials, and chiral resolution of a racemic multi-steps reaction product using an appropriate chiral reagent are two traditional strategies.[2b-c, 4] However, expensive prices of chiral materials and a limited range of substrates limited the application of these two strategies. Recently, an attractive strategy which can generate a wide scope of 1,2-diarylethylenediamines, catalytic asymmetric nitro-Mannich reaction of aromatic aldimines with α-aryl nitromethanes followed by the reduction of nitro group, has been developed.[5] Although a series of asymmetric nitro-Mannich reaction of nitromethane and its alkyl congeners have been successfully reported,[6] to the best of our knowledge, the successful asymmetric nitro-Mannich reactions using α-aryl nitromethanes as substrates are rare. There are two research efforts that are impressive. One of them was reported by Johnston and co-workers in 2011.[7] In this work, chiral bisamidine-quinoline catalysts were found to be efficient in the asymmetric addition of α-aryl nitromethanes to *N*-Boc aldimines, and aza-Henry adducts were obtained in good yields with good to high diastereo- and enantioselectivities (2:1->20:1 dr and 76-93% ee) (Scheme 1a). In another work reported by Ooi's group, chiral ammonium betaines were successfully used to catalyze the highly diastereo- and enantioselective nitro-Mannich reaction of α-aryl nitromethanes with *N*-Boc imines. However, the reaction should be carried out under stringent anhydrous conditions[8] (Scheme 1b). Although these elegant works have

Scheme 1. Previously reported asymmetric nitro-Mannich reaction of *N*-Boc imines with α-aryl nitromethanes, and a new method with respect to this reaction.

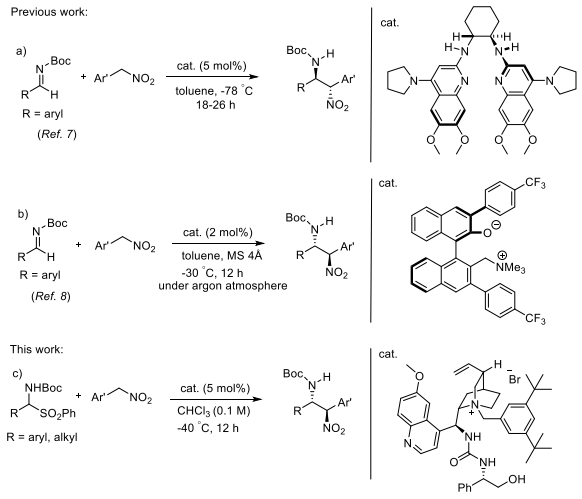
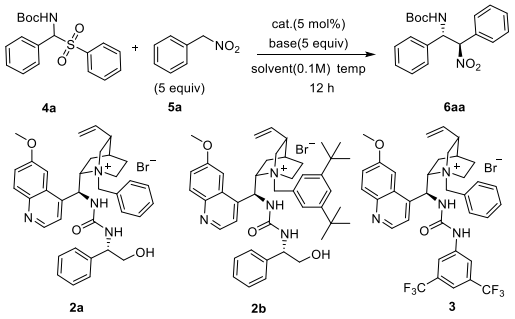


Table 1. Optimization of Reaction Conditions[a]



entry	cat.	solvent	base	temp (℃)	yield[b] (%)	d.r.[c]	ee[d]
1	**2a**	toluene	KOH	-30	67	96:4	71
2	**2a**	toluene	K_2CO_3	-30	43	94:6	70
3	**2a**	toluene	Cs_2CO_3	-30	56	98:2	68
4	**2a**	toluene	LiOH	-30	93	98:2	74
5	**2b**	toluene	LiOH	-30	98	98:2	87
6	**3**	toluene	LiOH	-30	84	97:3	72
7	**2b**	CH_2Cl_2	LiOH	-30	85	99:1	98
8	**2b**	$CHCl_3$	LiOH	-30	99	99:1	95
9	**2b**	$CHCl_3$	LiOH	-40	99	99:1	99
10[e]	**2b**	$CHCl_3$	LiOH	-40	85	98:2	91
11[f]	**2b**	$CHCl_3$	LiOH	-40	95	99:1	98
12[g]	**2b**	$CHCl_3$	LiOH	-40	99	99:1	99
13[h]	**2b**	$CHCl_3$	LiOH	-40	92	99:1	99

[a]Unless otherwise noted, Reactions were carried out with 0.1 mmol of **4a**, 0.5 mmol of **5a**, and 5 mol% of catalyst in 1.0 mL of solvent. [b]Yield of isolated product. [c]Diastereomeric ratios determined by ^{1}H NMR. [d]Determined by HPLC using a chiral stationary phase. [e]1 mol% catalyst was used. [f]2.5 mol% catalyst was used. [g]0.15 mmol of **5a** was used. [h]0.11 mmol of **5a** was used.

been reported, in terms of α-aryl nitromethanes and the corresponding adducts containing acidic hydrogen atoms at benzyl position, developing an efficient base-catalyzed highly diastereo- and enantioselective catalytic system is still challenging and desirable.[8,9]

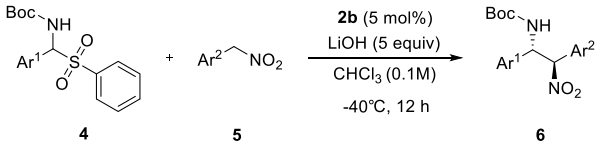
Amidosulfones due to their broad range and good stability compared with the *N*-Boc imines have been used in several asymmetric catalytic reactions.[6c,6d,10] In our previous work, amidosulfones successfully reacted with nitroalkanes in the presence of the bifunctional phase transfer catalyst **2a**.[11a] Enlightened by this work and as a continuation of our studies on developing bifunctional chiral phase transfer catalysts bearing multiple H-bond donors, we anticipated that a similar protocol could be applied to the asymmetric nitro-Mannich reaction of α-aryl nitromethanes, albeit controlling diastereo- and enantioselectivity that would be significantly more challenging. Herein, we would like to report an efficient and highly diastereo- and enantioselective nitro-Mannich reaction of *N*-Boc amidosulfones with α-aryl nitromethanes catalyzed by a novel phase transfer catalyst bearing multiple H-bonding donors. (Scheme 1c).

RESULTS AND DISCUSSION

In order to evaluate the catalytic potential of chiral phase transfer phase catalysts in the asymmetric nitro-Mannich reaction of α-aryl nitromethanes, we initially chose the reaction of amidosulfone **4a** with α-phenyl nitromethane **5a** as a model reaction (Table 1), and investigated the catalytic activity of catalyst **2a**. Gratifyingly, in the presence of KOH and toluene at -30 ℃, catalyst **2a** showed a good asymmetric catalytic activity, and the desired adduct **6aa** (1S, 2R) was isolated in 67% yield with 96:4 dr and 71% ee (entry 1), The product configuration is in agreement with the data reported in the literature.[7] In further screening of bases, K_2CO_3 and Cs_2CO_3 have no apparent improvement in the yield and ee value of the product (entries 2-3). Surprisingly, when LiOH was employed in the reaction, the yield of **6aa** increased from 67% to 93%, and the dr and ee values were also improved slightly (entry 4). Inspired by these good results, we turned our attention on the modification of catalyst on the basis of catalyst **2a**. To this end, catalyst **2b** was synthesized using sterically hindered 3,5-di-*tert*-butyl benzyl in place of benzyl on the nitrogen atom of quinine according to the procedure described in our previous work.[11] Remarkably, catalyst **2b** exhibited an improved asymmetric catalytic activity and stereoselectivity in the presence of LiOH and using toluene as the reaction solvent (entry 5). In addition, well-behaved catalyst **3**, which was developed by Dixon group and exhibited excellent asymmetric activity in the nitro-Mannich reaction of nitromethane, was also evaluated under the identical reaction conditions. Compared with catalyst **2b**, it did not have a positive impact on the yield and enantioselectivity (entry 6), and the relative and absolute configurations of the product is consistent. In subsequent screening of solvents and reaction temperatures, dichloromethane used as the solvent have a beneficial effect on the enantioselectivity of adduct **6aa**, and the ee value increased from 87% to 98% at -30 ℃. However, the yield decreased to 85% (entry 7). On the contrary, chloroform led to a high yield but ee value decreased slightly at -30 ℃ (entry 8). Lowering the reaction temperature to -40 ℃ further improved the reaction results. In this case, catalyst **2b** exhibited excellent catalytic activity and diastereo- and enantiocontrolling ability (entry 9, 99% yield, 99:1 dr, 99% ee). In the final optimization of loadings of catalyst **2b** and substrate **4a**, lowering catalyst **2b** loadings led to a decrease in the yield (entries 10 and 11). Satisfyingly, reducing the amounts of substrate **4a** from 5 to 1.5 equiv., we can still get the best result (entry 12). However, performing this reaction with 1.1 equiv. of **4a** led to a slight decline in the yield (entry 13). After a series of screenings and optimizations, eventually, the optimal reaction conditions were identified as follows: 1.5 equiv. of **4a**, 5 mol% of catalyst **2b**, 5 equiv. of LiOH, $CHCl_3$ used as solvent, the reaction temperature of -40 ℃ and 12 h.

With the optimal conditions in hand, the scope of the reaction with respect to amidosulfones and α-aryl nitromethanes were investigated, and corresponding results were summarized in Table 2. For all cases, excellent yields (90-99%), excellent diastereo- and enantioselectivities (93:7-99:1 dr, 91-99% ee) were obtained across the series. In these cases, a variety of amidosulfones derived from aromatic aldehydes proved effective, with an electron-donating or electron-withdrawing group in *ortho*-, *meta*- as well as *para*-position all being well-tolerated with excellent reactivity and stereoseclectivities observed (entries 1-12). In spite of this, in terms of methoxyl-substituted amidosulfones, the position of methoxy have a slight effect on the diastereoselectivity. For example, compared with substrates **4c** and **4j**, *meta*-methoxy-substituted amidosulfone **4d** afforded adduct **6da** with a slightly decreased dr (93:7) (entry

Table 2. Substrate Scope of Nitro-Mannich Reaction Using Catalyst 2b[a]



entry	4	Ar^1	5	Ar^2	6	yield[b] (%)	d.r.[c]	ee[d] (%)
1	**4b**	*o*-FC_6H_4	**5a**	Ph	**6ba**	99	>99:1	99[e]
2	**4c**	*o*-$MeOC_6H_4$	**5a**	Ph	**6ca**	99	99:1	98
3	**4d**	*m*-$MeOC_6H_4$	**5a**	Ph	**6da**	99	93:7	98[e]
4	**4e**	*m*-ClC_6H_4	**5a**	Ph	**6ea**	99	>99:1	98
5	**4f**	*p*-FC_6H_4	**5a**	Ph	**6fa**	99	98:2	98[f]
6	**4g**	*p*-ClC_6H_4	**5a**	Ph	**6ga**	99	>99:1	99[f]
7	**4h**	*p*-BrC_6H_4	**5a**	Ph	**6ha**	97	>99:1	99[e]
8	**4i**	*p*-MeC_6H_4	**5a**	Ph	**6ia**	99	>99:1	96[f]
9	**4j**	*p*-$MeOC_6H_4$	**5a**	Ph	**6ja**	99	99:1	98[f]
10	**4k**	*p*-$CF_3C_6H_4$	**5a**	Ph	**6ka**	99	>99:1	98[f]
11	**4l**	*p*-$NO_2C_4H_6$	**5a**	Ph	**6la**	93	94:6	99
12	**4m**	*p*-CNC_4H_6	**5a**	Ph	**6ma**	97	98:2	95
13	**4n**	2-naphthyl	**5a**	Ph	**6na**	90	>99:1	97[f]
14	**4o**	2-furyl	**5a**	Ph	**6oa**	99	98:2	99[e]
15	**4p**	2-thienyl	**5a**	Ph	**6pa**	99	97:3	92
16	**4a**	Ph	**5b**	*o*-FC_6H_4	**6ab**	94	93:7	99[e]
17	**4a**	Ph	**5c**	*m*-$MeOC_6H_4$	**6ac**	99	99:1	98[e]
18	**4a**	Ph	**5d**	*p*-BrC_6H_4	**6ad**	99	98:2	99[e]
19	**4a**	Ph	**5e**	*p*-MeC_6H_4	**6ae**	99	>99:1	99[e]
20	**4a**	Ph	**5f**	*p*-$MeOC_6H_4$	**6af**	99	99:1	91[e,f]
21	**4a**	Ph	**5g**	2-naphthyl	**6ag**	99	98:2	96[e,f]
22	**4j**	*p*-$MeOC_6H_4$	**5b**	*o*-FC_6H_4	**6jb**	98	99:1	98[e]
23	**4j**	*p*-$MeOC_6H_4$	**5d**	*p*-BrC_6H_4	**6jd**	96	97:3	96[e]
24	**4h**	*p*-BrC_6H_4	**5d**	*p*-BrC_6H_4	**6hd**	99	97:3	99
25[g]	**4a**	Ph	**5a**	Ph	**6aa**	99	99:1	99[e]

[a]Unless otherwise noted, Reactions were carried out with 0.1 mmol of **4**,0.15 mmol of **5**, and 5 mol% of **2b** in 1.0 mL of $CHCl_3$. [b]Yield of isolated product. [c]Diastereomeric ratios determined by HPLC. [d]Determined by HPLC using a chiral stationary phase. [e,f]Absolute and relative configurations of anti-isomers were determined by comparison to literature data.[7,8] [g]The reaction was performed with 3.0 mmol of **4a**, 4.50 mmol of **5a**, and 5 mol% of **2b** in 30 mL of $CHCl_3$.

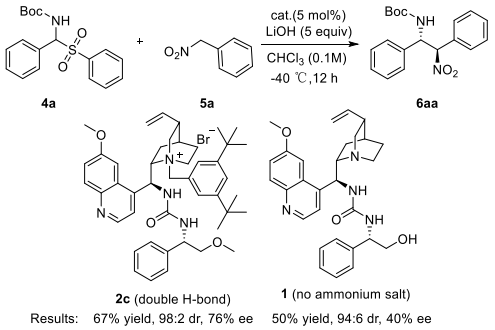
2,9 vs 3). Unfortunately, the desired product was not detected when the aminosulfone derived from 4-dimethylamino benzaldehyde was used as the substrate. Moreover, polycyclic aromatic and heteroaromatic substrates were also proved effective (entries 13-15). Next, we set out to investigate the generality of the reaction with other α-aryl nitromethanes. Pleasingly, the present catalytic system was applicable to a range of α-aryl nitromethanes with an electron-withdrawing or electron-donating group, and corresponding products were yielded in high yields (94-99%) with excellent dr and ee values (93:7-99:1 dr, 91-99% ee, entries 16-19). In addition, 1-(2-naphthyl) nitromethane **5g** used as the substrate also proved effective (entry 21, 98:2 dr and 96% ee). Similarly, arbitrary combinations of amidosulfones and α-aryl nitromethanes were well accommodated (entries 22 and 23), and products containing underlying symmetric 1,2-diarylethylenediamines scaffold could be obtained in high yields (entry 24). Subsequently, we have successfully conducted a gram scale reaction of **4a** with **5a** under standard conditions, and optically pure **6aa** was obtained after column chromatography (1.03 g, 99% yield, 99:1 dr and 99% ee, entry 25).

To investigate the role of the quaternary ammonium center and multiple H-bonding donors in this kind of bifunctional catalysts, and to test their synergistic catalysis, two control experiments were performed using compounds **2c** and **1** as catalysts respectively (Scheme 2). Compared with catalyst **2b**, catalyst **2c**, in which the hydroxyl group was protected by methylation, has lower catalytic activity and stereocontrol ability. Similarly, catalyst **1**, in absence of a quaternary ammonium center, exhibited a significant decrease in catalytic activity and diastereo- and enantiocontrol ability, and configurations of the product is consistent. These results supported synergistic catalysis of bifunctional catalysts and indicated that both the hydroxy on the phenylglycinol moiety and the quaternary ammonium center were crucial to achieve excellent catalytic activity and stereoselectivity in this asymmetric nitro-Mannich reaction.

To explain the stereoselectivity of the reaction, a possible transition-state model was proposed (Figure 1). The ammoni-

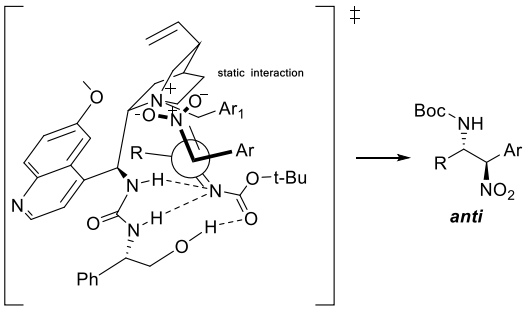
um motif pairs with the nitro compounds by electrostatic interaction and the urea motif captures the *N*-Boc imines by hydrogen bond (HB) interaction. Therefore, a highly ordered transition state is formed and the nitro compounds can attack the *N*-Boc imines from the *Re* face.

Scheme 2. Control Experiment for Mechanistic Study.

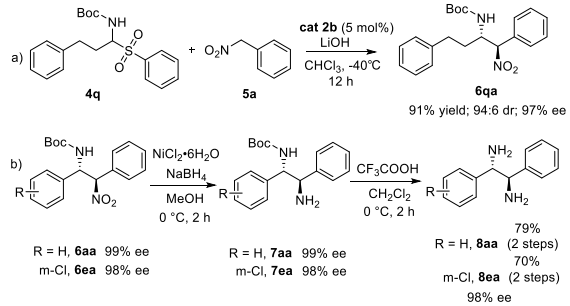


The universality of the present system was further demonstrated by the application to aliphatic amidosulfone, excellent levels of diastereo- and enantioselectivity were also obtained with amidosulfone **4q** as a substrate (Scheme 3a). Finally, the applicability of this protocol was demonstrated by the derivatization of optically pure **6aa** and **6ea**. As shown in scheme 3b, **6aa** could be readily derivatized into *meso*-symmetric 1,2-diarylethylenediamine **8aa**, and **6aa** could be coverted to unsymmetric *anti*-1,2-diarylethylenediamine **8ea** via a nickel-boride mediated reduction of nitro-group followed by the removal of Boc in the presence of trifluoroacetic acid.

Figure 1. Proposed transition state model leading to *anti*-adducts.



Scheme 3. Reaction of aliphatic amidosulfone with α-phenyl nitromethane, and derivatization of 6aa and 6ea to the corresponding 1,2-diarylethylenediamine 8aa and 8ea.



CONCLUSIONS

In summary, we have developed an efficient and highly diastereo- and enatioselective nitro-Mannich reaction of α-aryl nitromethanes with stable amidosulfones in place of *N*-Boc imines, which was catalyzed by a novel bifunctional phase-transfer catalyst bearing multiple H-bonding donors. A variety of α-aryl nitromethanes and amidosulfones were investigated, and corresponding products were obtained in excellent yields with excellent diastereo- and enantioselectivities. Using this asymmetric catalytic protocol, optically pure unsymmetric and *meso*-symmetric 1,2-diarylethylenediamines could be synthesized. Detail mechanism study on this reaction, and further application of this kind of bifunctional phase transfer catalysts bearing multiple H-donors are underway in our laboratory.

EXPERIMENTAL SECTION

General Information

Unless otherwise stated, all reagents were purchased from commercial suppliers and used without purification. All solvents were obtained from commercial sources and were purified according to standard procedures. For thin-layer chromatography (TLC), silica gel plates (HSGF 254) were used and compounds were visualized by irradiation with UV light. Purification of reaction products was carried out by flash column chromatography using silica gel (200-300 mesh).^{1}H and ^{13}C NMR, ^{19}F NMR spectra were recorded on a Varian Mercury-300BB (300 MHz); a Bruker NMR Spectrometer (400 MHz) or a Bruker NMR Spectrometer (500 MHz). All chemical shifts (δ) were given in ppm. Chemical shifts (δ ppm) are relative to the resonance of the deuterated solvent as the internal standard ($CDCl_3$, δ 7.26 ppm for proton NMR, δ 77.2 ppm for carbon NMR; CD_3OD-d_4, δ 3.31 ppm for proton NMR, δ 49.0 ppm for carbon NMR; DMSO-d_6, δ 2.50 ppm for proton NMR, δ 39.5 ppm for carbon NMR). Data are presented as follows: chemical shift, integration, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet) and coupling constant in Hertz (Hz). Mass spectra were recorded on the Bruker Agilent1290 MicrOTOF Q II. Melting points were measured on a melting point apparatus and were uncorrected. The ee values determination was carried out using chiral HPLC (Waters) with Chiracel IA-3 column, Chiracel IC-3 column and Chiracel AD-H column. Optical rotations were measured on a Shanghai ShenGuang SGW-2 Polarimeter at λ = 589 nm. Optical rotations are reported as follows: $[\alpha]_D^{20}$ (c=g/100 mL, solvent).

Starting materials

9-amino(9-deoxy)epicinchona alkaloids of quinine were prepared according to reported procedure.[12] All amidosulfones were prepared using reported procedures from corresponding aldehydes.[13] Nitro compounds were prepared by following the literature.[14] All aminoalcohols was purchased from commercial suppliers and used directly.

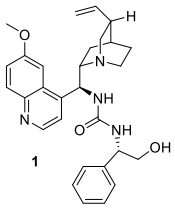
Preparation and characterization of the chiral ureas with multiple Hydrogen-Bonding Donors.

General Procedure:

N, N'-carbonyldiimidazole (165 mg, 1.02 mmol, 1.1 equiv) was dissolved in anhydrous THF, a solution of 9-amino(9-deoxy)epiquine (300 mg, 0.93 mmol, 1equiv) in THF (5 ml) was added dropwise in 1 h, the reaction mixture was stirred for another 1 h. Then aminoalcohol (1.1 equiv) and triethylamine (142ul, 1.1 equiv) were added in one portion respectively, the resulting mixture was stirred until TLC showed that the reaction was completed. The mixture was diluted with 36 ml ethylacetate, then washed with water (10×15ml), the organic phase was dried over Na_2SO_4. The solvent was removed under

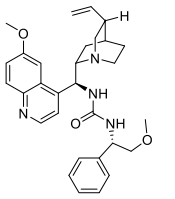
reduced pressure and the crude product was purified by flash chromatography (ethylacetate/MeOH=10:1).

Urea 1 derived from quinine and L-phenylglycinol / [**(S)-(+)-2-Phenylglycinol**]



Light yellow solid, 334 mg, 74% yield, m.p. =109-111 ℃, $[a]_D^{25}$ = -21 (c = 0.33, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ 8.64 (d, *J* = 4.6 Hz, 1H), 7.99 (d, *J* = 9.2 Hz, 1H), 7.64 (d, *J* = 2.3 Hz, 1H), 7.35 (dd, *J* = 9.1, 2.6 Hz, 1H), 7.30 – 7.25 (m, 3H), 7.21 – 7.11 (m, 3H), 6.25 (br. s, 1H), 5.87 (br. s, 1H), 5.79 – 5.53 (m, 1H), 5.22 (br. s, 1H), 5.09 – 4.86 (m, 2H), 4.64 (d, *J* = 5.2 Hz, 1H), 3.92 (s, 3H), 3.73 (d, *J* = 4.8 Hz, 2H), 3.16 (br. s, 2H), 3.03 – 2.85 (m, 1H), 2.75 – 2.36 (m, 2H), 2.24 (br. s, 1H), 1.72 – 1.30 (m, 4H), 1.01 – 0.77 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.2, 157.9, 147.5, 144.7, 141.2, 140.9, 140.5, 131.6, 128.9, 128.6, 128.4, 127.4, 126.7, 121.8, 114.9, 102.0, 66.9, 60.5, 57.2, 55.7, 55.5, 40.7, 39.2, 34.4, 27.5, 27.3, 26.0. HRMS (ESI): calculated for $C_{29}H_{35}N_4O_3$ $[M+H]^{+:}$ 487.2704, found 487.2695.

Urea derived from quinine and (1S)-2-Methoxy-1-phenylethanamine



Light yellow solid, 306 mg, 66% yield, m.p. = 90-91 ℃, $[a]_D^{25}$ = -25.2 (c = 0.5, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ 8.69 (d, *J* = 4.6 Hz, 1H), 8.01 (d, *J* = 9.2 Hz, 1H), 7.66 (d, *J* = 2.6 Hz, 1H), 7.37 (dd, *J* = 9.2, 2.7 Hz, 1H), 7.28 (d, *J* = 1.4 Hz, 1H), 7.25 – 7.17 (m, 5H), 6.34 (br.s, 1H), 5.78 – 5.59 (m, 1H), 5.51 (d, *J* = 6.7 Hz, 1H), 5.25 (br.s, 1H), 5.07 – 4.91 (m, 2H), 4.83 (dd, *J* = 11.4, 6.2 Hz, 1H), 3.95 (s, 3H), 3.57 – 3.40 (m, 2H), 3.37 – 3.14 (m, 6H), 2.90 – 2.64 (m, 2H), 2.45 – 2.25 (m, 1H), 1.77 – 1.59 (m, 3H), 1.53 – 1.37 (m, 1H), 1.06 – 0.94 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.7, 147.4, 145.7, 144.6, 141.1, 140.6, 131.5, 129.8, 128.4, 128.2, 127.4, 127.1, 126.5, 121.5, 114.5, 102.0, 75.6, 71.7, 60.0, 58.6, 55.7, 55.5, 53.9, 40.7, 39.3, 27.6, 27.3, 25.9. HRMS (ESI): calculated for $C_{30}H_{37}N_4O_3$ $[M+H]^+$: 501.2860, found 501.2844.

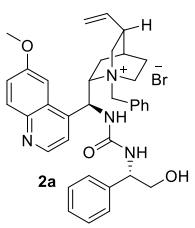
Preparation and characterization of the chiral PTC with multiple Hydrogen-Bongding donors

General Procedure:

Under N_2 protection, 9-amino(9-deoxy)epiquine-derived urea 1 (150 mg, 1 eq.)was dissolved in THF (0.1 M), then benzyl bromide (1.1 eq.) was added, the mixture was heated to reflux, after 12 h the mixture was concentrated and purified by flash chromatography.

Catalyst 2a

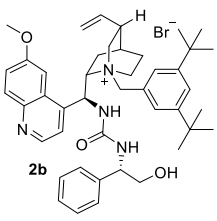
Obtained according to the general procedure, the crude product was purified by flash chromatography (Et_2O/MeOH=10:1).



Light yellow solid, 87 mg, 43 % yield, m.p. =178-179 ℃ (decomp.), $[a]_D^{25}$ = -44.4 (c = 0.5, $CHCl_3$). ^1H NMR (300 MHz, CD_3OD) δ 8.77 (d, *J* = 4.1 Hz, 1H), 8.01 (d, *J* = 9.2 Hz, 1H), 7.81 – 7.63 (m, 2H), 7.60 – 7.32 (m, 7H), 7.28 – 7.14 (m, 2H), 7.13 – 6.95 (m, 2H), 6.32 (d, *J* = 10.6 Hz, 1H), 5.98 – 5.71 (m, 1H), 5.34 – 5.05 (m, 3H), 5.03 – 4.96 (m, 1H), 4.44 – 4.24 (m, 1H), 4.20 – 3.88 (m, 4H), 3.81 – 3.37 (m, 5H), 2.84 – 2.56 (m, 1H), 2.25 – 1.72 (m, 5H), 1.22 – 1.07 (m, 1H). ^{13}C NMR (101 MHz, CD_3OD) δ 160.6, 158.7, 148.6, 148.3, 145.6, 145.4, 142.2, 137.5, 134.7, 131.9, 131.5, 130.4, 129.4, 128.8, 128.4, 128.2, 128.0, 127.4, 124.2, 124.0, 120.6, 118.2, 102.6, 69.4, 67.3, 66.4, 61.6, 58.1, 56.6, 51.5, 50.4, 38.6, 28.7, 28.1, 25.5. HRMS (ESI): calculated for $C_{36}H_{41}N_4O_3$ $[M-Br]^+$: 577.3173, found 577.3167.

Catalyst 2b

Obtained according to the general procedure, the crude product was purified by flash chromatography (Et_2O/MeOH=10:1).

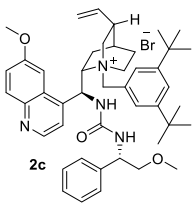


Light yellow solid, 115 mg, 48 % yield, m.p. =147-148 ℃ (decomp.), $[a]_D^{25}$ = -90.8 (c = 0.5, $CHCl_3$).

^1H NMR (500 MHz, CD_3OD) δ 8.72 (d, *J* = 45.6 Hz, 1H), 8.00 (d, *J* = 9.1 Hz, 1H), 7.81 – 7.59 (m, 3H), 7.55 – 7.43 (m, 1H), 7.30 (s, 2H), 7.13 (s, 2H), 7.02 – 6.58 (m, 3H), 6.32 (d, *J* = 10.0 Hz, 1H), 6.06 – 5.81 (m, 1H), 5.21 (dd, *J* = 19.5, 14.3 Hz, 2H), 4.91 (d, *J* = 11.8 Hz, 3H), 4.80 (br, J = 34.7 Hz, 1H), 4.34 (s, 1H), 4.19 (s, 1H), 4.06 (s, 3H), 3.70 – 3.34 (m, 5H), 2.70 (br, 1H), 2.25 – 1.72 (m, 4H), 1.39 (s, 2H), 1.34 (s, 18H), 1.14 (d, *J* = 13.3 Hz, 1H). ^{13}C NMR (126 MHz, CD_3OD) δ 160.6, 158.7, 153.2, 148.6, 146.0, 145.5, 141.9, 138.0, 131.9, 129.3, 129.0, 128.7, 128.2, 128.1, 127.2, 125.8, 124.3, 120.8, 118.2, 102.4, 70.2, 68.0, 66.6, 61.2, 57.7, 56.6, 51.0, 50.2, 38.6, 35.8, 31.8, 29.1, 28.1, 25.6. HRMS (ESI): calculated for $C_{44}H_{57}N_4O_3$ $[M-Br]^+$: 689.4425, found 689.4425.

Catalyst 2c.

Obtained according to the general procedure, the crude product was purified by flash chromatography (EA /MeOH=10:1).



Light yellow solid, 146 mg, 62 % yield, m.p. =167-168 ℃, $[a]_D^{25}$ = -25.5 (c = 0.33, $CHCl_3$). ^1H NMR (300 MHz, CD_3OD) δ 8.77 (d, *J* = 4.7 Hz, 1H), 8.01 (d, *J* = 9.2 Hz, 1H), 7.65 (d, *J* = 15.0 Hz, 3H), 7.55 – 7.43 (m, 1H), 7.29 (s, 2H), 7.14 (d, *J* = 6.9 Hz, 2H), 6.94 (d, *J* = 7.4 Hz, 3H), 6.31 (d, *J* = 10.6 Hz, 1H), 5.99 – 5.87 (m, 1H), 5.28 – 5.13 (m, 2H), 5.03 – 4.92 (m, 2H), 4.88 – 4.78 (m, 1H), 4.40 (br, 1H), 4.19 (br, 1H), 4.07 (s, 3H), 3.77 – 3.53 (m, 2H), 3.48 (dd, *J* = 10.0, 4.4 Hz, 2H), 3.42 – 3.32 (m, 2H), 3.13 (s, 3H), 2.71 (d, *J* = 6.2 Hz, 1H), 2.26 – 1.93 (m, 4H), 1.88 (br, 2H), 1.33 (s, 18H). ^{13}C NMR (75 MHz, CD_3OD) δ 160.8, 158.8, 153.4, 148.7, 146.0, 145.8, 141.9, 138.0, 132.1, 129.4, 129.1, 128.8, 128.3, 127.9, 127.3, 125.9, 124.3, 120.8, 118.3, 102.7, 77.0, 70.2, 68.2, 61.5, 59.2, 56.7, 55.5, 51.4, 50.4, 38.7, 36.0, 31.9, 29.2, 28.3, 25.8. HRMS (ESI): calculated for $C_{45}H_{59}N_4O_3$ $[M-Br]^+$: 703.4582, found 703.4569.

General procedure for enantio- and diastereoselective nitro-Mannich reaction

Without protection of inert gases, catalyst **2b** (5 mol%) and amidosulfones (0.10 mmol) were dissolved in dry chloroform (1.0 mL), α-Aryl nitromethane (0.15 mmol, 1.5 eq.) was added, the mixture was cooled to –40 °C, freshly grounded LiOH (12.0 mg, 5 eq.) was added in one portion, the resulting suspention was vigorously stirred at –40 °C. After 12 h, 5 ml sat.

aq. NH_4Cl was added and the solution was allowed to warm to room temperature, the aqueous was extracted with ethylacetate (3×5ml), then the organic layer was dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography (PE/EA=10:1).

Synthesis of racemates:

Without protection of inert gases, amidosulfones (0.10 mmol) were dissolved in dry chloroform (1.0 mL), α-Aryl nitromethane (0.15 mmol, 1.5 eq.) was added, the mixture was stirred at room temperature, DBU(20 mol%) was added. After 12 h, 5 mL sat. aq. NH_4Cl was added, the aqueous was extracted with ethylacetate (3×5 mL), then the organic layer was dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography (PE/EA=10:1).

Tert-butyl [(1S,2R)-2-nitro-1,2-diphenylethyl]carbamate (6aa)

White solid, 34 mg, 99% yield, dr=99:1, m.p. =198-200 ℃, $[a]_D^{20}$ = 49.2 (c = 0.5, $CHCl_3$), The ee value was 99% [Chiralpak IA-3, hexane/i-PrOH = 90:10, 210 nm, 1.0 mL/min, Major-anti-(t_{major} =17.74 min., t_{minor} =16.11min), Minor-syn-(t_{major} =25.23 min., t_{minor} =12.24 min)]. ^1H NMR (300 MHz, $CDCl_3$) δ 7.62 – 7.52 (m, 3H), 7.49 – 7.39 (m, 3H), 7.38 – 7.24 (m, 4H), 5.74 (br, 1H), 5.63 (br, 1H), 4.84 (s, 1H), 1.26 (s, 9H). Analytical and spectral data were in agreement with the literature data.[8]

Tert-butyl [(1S,2R)-1-(2-fluorophenyl)-2-nitro-2-phenylethyl]carbamate (6ba)

White solid, 35.8 mg, 99% yield, dr=99:1, m.p. =181-183 ℃, $[a]_D^{20}$ = 56.8 (c = 0.5, CHCl3), The ee value was 99% [Chiralpak IC-3, hexane/EtOH = 16:1, 210 nm, 0.5 mL/min, Major-anti-(t_{major} =12.12 min., t_{minor} =13.27 min), Minor-syn-(t_{major} =18.67 min., t_{minor} =15.16 min)]. ^1H NMR (300 MHz, $CDCl_3$) δ7.63 (dd, *J* = 6.5, 3.1 Hz, 2H), 7.53 – 7.29 (m, 5H), 7.21 – 7.02 (m, 2H), 5.87 (d, *J* = 3.6 Hz, 2H), 5.07 (br, 1H), 1.22 (s, 9H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -117.2 Analytical and spectral data were in agreement with the literature data.[8]

Tert-butyl [(1S,2R)-1-(2-methoxyphenyl)-2-nitro-2-phenylethyl]carbamate (6ca)

White solid, 37 mg, 99% yield, dr=99:1, m.p. =185-187 ℃, $[a]_D^{20}$ = 59.2 (c = 0.5, $CHCl_3$), The ee value was 98% [Chiralpak IA-3, hexane/i-PrOH = 90:10, 210 nm, 1.0 mL/min, Major-anti-(t_{major} =8.73min., t_{minor} =27.67 min), Minor-syn-(t_{major} =10.06 min., t_{minor} =17.63 min)]. ^1H NMR (300 MHz, $CDCl_3$) δ 7.64 (s, 2H), 7.40 (s, 3H), 7.35 – 7.22 (m, 2H), 7.02 – 6.83 (m, 2H), 5.99 (d, *J* = 7.2 Hz, 1H), 5.81 (t, *J* = 10.4 Hz, 1H), 5.51 (d, *J* = 10.4 Hz, 1H), 3.98 (s, 3H), 1.20 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.2, 154.4, 132.0, 131.5, 130.1, 129.9, 128.96, 128.5, 124.4, 121.3, 111.2, 93.2, 79.7, 55.9, 55.6, 28.1. HRMS (ESI): calculated for $C_{20}H_{24}N_2O_5Na^+$ ([M+Na]$^+$) 395.1577. Found 395.1577. Absolute and relative configurations were assigned on the analogy of **6aa.**

Tert-butyl [(1S,2R)-1-(3-methoxyphenyl)-2-nitro-2-phenylethyl]carbamate (6da)

White solid, 37.1 mg, 99% yield, dr=93:7, m.p. =177-178 ℃, $[a]_D^{20}$ = 43 (c = 0.4, $CHCl_3$), The ee value was 98% [Chiralpak IA-3, hexane/i-PrOH = 90:10, 210 nm, 1.0 mL/min, Major-anti-(t_{major} =21.75 min., t_{minor} =31.58 min), Minor-syn-(t_{major} =18.77 min., t_{minor} =16.02 min)]. ^1H NMR (300 MHz, $CDCl_3$) δ 7.64 – 7.51 (m, 2H), 7.47 – 7.35 (m, 3H), 7.32 – 7.22 (m, 2H), 6.95 – 6.82 (m, 2H), 5.75 (d, *J* = 9.9 Hz, 1H), 5.61 (t, *J* = 9.4 Hz, 1H), 4.72 (d, *J* = 9.4 Hz, 1H), 3.80 (s, 3H), 1.25 (s, 9H). Analytical and spectral data were in agreement with the literature data.[8]

Tert-butyl [(1S,2R)-1-(3-chlorophenyl)-2-nitro-2-phenylethyl]carbamate (6ea)

White solid, 37.3 mg, 99% yield, dr=99:1, m.p. =192-194 ℃, $[a]_D^{20}$ = 33.6 (c = 0.5, $CHCl_3$), The ee value was 98% [Chiralpak IA-3, hexane/i-PrOH = 90:10, 210 nm, 1.0 mL/min, Major-anti-(t_{major} =12.34 min., t_{minor} =13.47 min), Minor-syn-(t_{major} =16.28 min., t_{minor} =9.81 min)]. ^1H NMR (300 MHz, $CDCl_3$) δ 7.60 – 7.49 (m, 2H), 7.47 – 7.39 (m, 3H), 7.37 – 7.28 (m, 3H), 7.25 – 7.21 (m, 1H), 5.71 (dd, *J* = 18.0 Hz, 2H), 4.85 (br, 1H), 1.26 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.19, 139.60, 134.87, 131.18, 130.39, 130.27, 128.97, 128.65, 127.44, 125.51, 93.93, 80.71, 56.33, 28.05. HRMS (ESI): calculated for $C_{19}H_{21}ClN_2NaO_4^+$ ([M+Na]$^+$) 399.1082. Found 399.1080. Absolute and relative configurations were assigned on the analogy of **6aa.**

Tert-butyl [(1S,2R)-1-(4-fluorophenyl)-2-nitro-2-phenylethyl]carbamate (6fa)

White solid, 36 mg, 99% yield, dr=98:2, m.p. =191-193 ℃, $[a]_D^{20}$ = 82.8 (c = 0.5, $CHCl_3$), The ee value was 98% [Chiralpak IA-3, hexane/EtOH = 95:5, 230 nm, 1.0 mL/min, Major-anti-(t_{major} =13.39 min., t_{minor} =12.74 min), Minor-syn-(t_{major} =15.60 min., t_{minor} =25.46 min)]. ^1H NMR (300 MHz, $CDCl_3$) δ 7.63 – 7.50 (m, 2H), 7.49 – 7.38 (m, 3H), 7.34 (dd, *J* = 8.6, 5.2 Hz, 2H), 7.14 – 6.98 (m, 2H), 5.76 (d, *J* = 10.1 Hz, 1H), 5.65 (d, *J* = 9.1 Hz, 1H), 4.79 (d, *J* = 8.8 Hz, 1H), 1.26 (s, 9H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -112.7. Analytical and spectral data were in agreement with the literature data.[7]

Tert-butyl [(1S,2R)-1-(4-chlorophenyl)-2-nitro-2-phenylethyl]carbamate (6ga)

White solid, 37.4 mg, 99% yield, dr=99:1, m.p.=196-197 ℃, $[a]_D^{20}$ = 24.8 (c = 0.5, $CHCl_3$), The ee value was 99% [Chiralpak AD-H, hexane/i-PrOH = 90:10, 214 nm, 1.0 mL/min, Major-anti-(t_{major} =21.14 min., t_{minor} =35.13 min), Minor-syn-(t_{major} =32.27 min., t_{minor} =22.89 min)]. ^1H NMR (300 MHz, $CDCl_3$) δ 7.59 – 7.49 (m, 2H), 7.48 – 7.38 (m, 3H), 7.38 – 7.26 (m, 4H), 5.76 (d, *J* = 9.8 Hz, 1H), 5.62 (d, *J* = 9.2 Hz, 1H), 4.76 (d, *J* = 9.0 Hz, 1H), 1.26 (s, 9H). Analytical and spectral data were in agreement with the literature data.[7]

Tert-butyl [(1S,2R)-1-(4-boranylphenyl)-2-nitro-2-phenylethyl]carbamate (6ha)

White solid, 40.8 mg, 97% yield, dr=99:1, m.p.=189-190 ℃, $[a]_D^{20}$ = 38 (c = 0.3, $CHCl_3$), The ee value was 99% [Chiralpak AD-H, hexane/i-PrOH = 95:5, 210 nm, 1.0 mL/min, Major-anti-(t_{major} =41.54 min., t_{minor} =29.64 min), Minor-syn-(t_{major} =55.38 min., t_{minor} =34.92 min)]. ^1H NMR (300 MHz, $CDCl_3$) δ 7.59 – 7.46 (m, 4H), 7.46 – 7.38 (m, 3H), 7.30 – 7.18 (m, 2H), 5.75 (d, *J* = 9.3 Hz, 1H), 5.61 (br, 1H), 4.81 (br, 1H), 1.26 (s, 9H). Analytical and spectral data were in agreement with the literature data.[8]

Tert-butyl [(1S,2R)-2-nitro-2-phenyl-1-(p-tolyl)ethyl]carbamate (6ia)

White solid, 35.4 mg, 99% yield, dr=99:1, m.p.=190-192 ℃, $[a]_D^{20}$ = 31.2 (c = 0.5, $CHCl_3$), The ee value was 96% [Chiralpak AD-H, hexane/i-PrOH = 90:10, 210 nm, 1.0 mL/min, Major-anti-(t_{major} =15.66 min., t_{minor} =14.40 min), Minor-syn-

(t_{major} =24.43 min., t_{minor} =11.97 min)]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.61 – 7.52 (m, 2H), 7.49 – 7.35 (m, 3H), 7.28 – 7.20 (m, 2H), 7.17 (d, *J* = 8.2 Hz, 1H), 5.75 (d, *J* = 10.1 Hz, 1H), 5.64 (br, 1H), 4.76 (d, *J* = 9.4 Hz, 1H), 2.34 (s, 3H), 1.24 (s, 9H). Analytical and spectral data were in agreement with the literature data.[8]

Tert-butyl [(1S,2R)-1-(4-methoxyphenyl)-2-nitro-2-phenylethyl]carbamate (6ja)

White solid, 37.1 mg, 99% yield, dr=99:1, m.p. =191-193 ℃, $[a]_D^{20}$ = 49.6 (c = 0.5, $CHCl_3$), The ee value was 98% [Chiralpak IA-3, hexane/i-PrOH = 90:10, 210 nm, 1.0 mL/min, Major-anti-(t_{major} =18.74 min., t_{minor} =60.96 min), Minor-syn-(t_{major} =33.19 min., t_{minor} =20.76 min)]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.65 – 7.52 (m, 2H), 7.42 (dd, *J* = 5.1, 2.0 Hz, 3H), 7.34 – 7.25 (m, 1H), 6.93 (d, *J* = 7.8 Hz, 1H), 6.90 – 6.82 (m, 2H), 5.76 (d, *J* = 9.9 Hz, 1H), 5.68 (d, *J* = 9.0 Hz, 1H), 4.75 (d, *J* = 9.0 Hz, 1H), 3.80 (s, 3H), 1.25 (s, 9H). Analytical and spectral data were in agreement with the literature data.[8]

Tert-butyl [(1S,2R)-2-nitro-2-phenyl-1-(4-(trifluoromethyl)phenyl)ethyl]carbamate (6ka)

White solid, 41.0 mg, 99% yield, dr=99:1, m.p. =191-193 ℃, $[a]_D^{20}$ = 54.8 (c = 0.5, $CHCl_3$), The ee value was 98% [Chiralpak IA-3, hexane/i-PrOH = 95:5, 210 nm, 1.0 mL/min, Major-anti-(t_{major} =37.53 min., t_{minor} =23.85 min), Minor-syn-(t_{major} =47.90 min., t_{minor} =33.23 min)]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.63 (d, *J* = 8.2 Hz, 2H), 7.58 – 7.52 (m, 2H), 7.52 – 7.38 (m, 5H), 5.79 (s, 1H), 5.73 (d, *J* = 8.6 Hz, 1H), 4.82 (d, *J* = 8.9 Hz, 1H), 1.26 (s, 9H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.7. Analytical and spectral data were in agreement with the literature data.[7]

Tert-butyl [(1S,2R)-2-nitro-1-(4-nitrophenyl)-2-phenylethyl]carbamate (6la)

White solid, 36.0 mg, 93% yield, dr=94:6, m.p. =187-188 ℃, $[a]_D^{20}$ = 22 (c = 0.4, $CHCl_3$), The ee value was 99% [Chiralpak IA-3, hexane/i-PrOH = 90:10, 210 nm, 1.0 mL/min, Major-anti-(t_{major} =24.73 min., t_{minor} =20.13 min), Minor-syn-(t_{major} =36.53 min., t_{minor} =27.63 min)]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 – 8.19 (m, 2H), 7.60 – 7.51 (m, 4H), 7.50 – 7.41 (m, 3H), 5.83 (br, 1H), 5.72 (t, *J* = 8.9 Hz, 1H), 4.88 (d, *J* = 8.5 Hz, 1H), 1.27 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.2, 148.0, 144.7, 130.8, 130.7, 129.2, 128.5, 128.4, 124.1, 93.5, 81.1, 56.3, 28.1. HRMS (ESI): calculated for $C_{19}H_{21}N_3NaO_6^+$ ([M+Na]$^+$) 410.1323. Found 410.1330. Absolute and relative configurations were assigned on the analogy of **6aa.**

Tert-butyl [(1S,2R)-1-(4-cyanophenyl)-2-nitro-2-phenylethyl]carbamate (6ma)

White solid, 35.7 mg, 97% yield, dr=98:2, m.p. =176-177 ℃, $[a]_D^{20}$ = 37 (c = 0.5, $CHCl_3$), The ee value was 95% [Chiralpak IA-3, hexane/i-PrOH = 90:10, 210 nm, 1.0 mL/min, Major-anti-(t_{major} =21.34 min., t_{minor} =19.77 min), Minor-syn-(t_{major} =32.67 min., t_{minor} =27.95 min)]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, *J* = 8.1 Hz, 2H), 7.60 – 7.39 (m, 7H), 5.79 (br, 1H), 5.68 (d, *J* = 8.1 Hz, 1H), 4.90 (br, 1H), 1.27 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.2, 142.8, 132.7, 130.8, 130.6, 129.2, 128.5, 128.2, 118.2, 112.8, 93.5, 81.0, 52.1, 28.0. HRMS (ESI): calculated for $C_{20}H_{21}N_3NaO_4^+$ ([M+Na]$^+$) 390.1424. Found 390.1425. Absolute and relative configurations were assigned on the analogy of **6aa.**

Tert-butyl [(1S,2R)-1-(naphthalen-2-yl)-2-nitro-2-phenylethyl]carbamate (6na)

White solid, 35.3 mg, 90% yield, dr=99:1, m.p. =190-191 ℃, $[a]_D^{20}$ = 23.5 (c = 0.4, $CHCl_3$), The ee value was 97% [Chiralpak IA-3, hexane/i-PrOH = 90:10, 210 nm, 1.0 mL/min, Major-anti-(t_{major} =23.21 min., t_{minor} =17.95 min), Minor-syn-(t_{major} =28.97 min., t_{minor} =14.68 min)]. ^{1}H NMR (300 MHz, CDCl3) δ 7.93 – 7.74 (m, 4H), 7.68 – 7.56 (m, 2H), 7.55 – 7.36 (m, 6H), 5.89 (s, 2H), 4.89 (d, *J* = 8.1 Hz, 1H), 1.25 (s, 9H). Analytical and spectral data were in agreement with the literature data.[8]

Tert-butyl [(1R,2R)-1-(furan-2-yl)-2-nitro-2-phenylethyl]carbamate (6oa)

White solid, 33 mg, 99% yield, dr=98:2, m.p. =163-165 ℃, $[a]_D^{20}$ = 44.8 (c = 0.5, $CHCl_3$), The ee value was 99% [Chiralpak IC-3, hexane/i-PrOH = 98:2, 210 nm, 1.0 mL/min, Major-anti-(t_{major} =22.69 min., t_{minor} =35.67 min), Minor-syn-(t_{major} =47.19 min., t_{minor} =40.83 min)]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.60 – 7.49 (m, 2H), 7.46 – 7.33 (m, 4H), 6.34 (d, *J* = 1.3 Hz, 2H), 5.83 (s, 2H), 4.88 (br, 1H), 1.26 (s, 9H). Analytical and spectral data were in agreement with the literature data.[8]

Tert-butyl [(1R,2R)-2-nitro-2-phenyl-1-(thiophen-2-yl)ethyl]carbamate (6pa)

White solid, 34.7 mg, 99% yield, dr=97:3, m.p. =166-167 ℃, $[a]_D^{20}$ =38.4 (c = 0.5, $CHCl_3$), The ee value was 92% [Chiralpak IC-3, hexane/EtOH = 16:1, 210 nm, 0.5 mL/min, Major-anti-(t_{major} =13.77 min., t_{minor} =15.11 min), Minor-syn-(t_{major} =19.71 min., t_{minor} =17.53 min)]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.61 – 7.48 (m, 2H), 7.47 – 7.35 (m, 3H), 7.33 – 7.21 (m, 1H), 7.06 (d, *J* = 3.4 Hz, 1H), 6.97 (dd, *J* = 5.1, 3.6 Hz, 1H), 5.95 (d, *J* = 9.4 Hz, 1H), 5.86 (d, *J* = 9.6 Hz, 1H), 4.79 (br, 1H), 1.28 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.1, 140.4, 131.5, 130.2, 128.9, 128.6, 127.1, 126.4, 125.8, 94.5, 80.6, 52.6, 28.1. HRMS (ESI): calculated for $C_{17}H_{20}N_2NaO_4S^+$ ([M+Na]$^+$) 371.1036. Found 371.1034. Absolute and relative configurations were assigned on the analogy of **6aa.**

Tert-butyl [(1S,2R)-2-(2-fluorophenyl)-2-nitro-1-phenylethyl]carbamate (6ab)

White solid, 33.8 mg, 94% yield, dr=93:7, m.p. =175-176 ℃, $[a]_D^{20}$ =25.6 (c = 0.5, $CHCl_3$), The ee value was 99% [Chiralpak IA-3, hexane/i-PrOH = 90:10, 210 nm, 0.5 mL/min, Major-anti-(t_{major} =33.81 min., t_{minor} =17.89 min), Minor-syn-(t_{major} =27.08 min., t_{minor} =19.56 min)]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80 (t, *J* = 7.0 Hz, 1H), 7.37 (s, 6H), 7.27 – 7.18 (m, 1H), 7.12 (t, *J* = 9.3 Hz, 1H), 6.21 (d, *J* = 10.4 Hz, 1H), 5.72 (br, 1H), 4.90 (d, *J* = 9.2 Hz, 1H), 1.23 (s, 9H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -117.9. Analytical and spectral data were in agreement with the literature data.[8]

Tert-butyl [(1S,2R)-2-(3-methoxyphenyl)-2-nitro-1-phenylethyl]carbamate (6ac)

White solid, 37.1 mg, 90% yield, dr=99:1, m.p. =179-181 ℃, $[a]_D^{20}$ = 22 (c = 0.5, $CHCl_3$), The ee value was 98% [Chiralpak IA-3, hexane/i-PrOH = 90:10, 210 nm, Major-anti-(t_{major} =40.56 min., t_{minor} =20.92 min), Minor-syn-(t_{major} =22.33 min., t_{minor} =16.54 min)]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43 – 7.27 (m, 6H), 7.17 – 7.08 (m, 2H), 7.01 – 6.92 (m, 1H), 5.73 (t, *J* = 13.6 Hz, 2H), 4.77 (br, 1H), 3.83 (s, 3H), 1.27 (s, 9H).

Analytical and spectral data were in agreement with the literature data.[8]

Tert-butyl [(1S,2R)-2-(4-bromophenyl)-2-nitro-1-phenylethyl]carbamate (6ad)

White solid, 42.1 mg, 99% yield, dr=98:2, m.p. =169-171 ℃, $[a]_D^{20}$ = 29.6 (c = 0.5, $CHCl_3$), The ee value was 99% [Chiralpak IA-3, hexane/i-PrOH = 90:10, 210 nm, 1.0 mL/min, Major-anti-(t_{major} =16.20 min., t_{minor} =20.86 min), Minor-syn-(t_{major} =43.19 min., t_{minor} =12.67 min)]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.55 (d, *J* = 8.0 Hz, 2H), 7.46 (d, *J* = 7.9 Hz, 2H), 7.41 – 7.22 (m, 5H), 5.74 (br, 1H), 5.63 (br, 1H), 4.85 (br, 1H), 1.27 (s, 9H). Analytical and spectral data were in agreement with the literature data.[8]

Tert-butyl [(1S,2R)-2-nitro-1-phenyl-2-(p-tolyl)ethyl]carbamate (6ae)

White solid, 35.5 mg, 99% yield, dr=99:1, m.p. =184-186 ℃, $[a]_D^{20}$ = 91.6 (c = 0.5, $CHCl_3$), The ee value was 99% [Chiralpak IA-3, hexane/i-PrOH = 90:10, 210 nm, 1.0 mL/min, Major-anti-(t_{major} =16.32 min., t_{minor} =15.14 min), Minor-syn-(t_{major} =25.18 min., t_{minor} =11.36 min)]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44 (d, *J* = 8.2 Hz, 2H), 7.40 – 7.30 (m, 5H), 7.21 (d, *J* = 7.9 Hz, 2H), 5.73 (d, *J* = 9.9 Hz, 1H), 5.66 (d, *J* = 8.4 Hz, 1H), 4.76 (br, 1H), 2.37 (s, 3H), 1.26 (s, 9H). Analytical and spectral data were in agreement with the literature data.[8]

Tert-butyl [(1S,2R)-2-(4-methoxyphenyl)-2-nitro-1-phenylethyl]carbamate (6af)

White solid, 37.1 mg, 99% yield, dr=99:1, m.p. =181-182 ℃, $[a]_D^{20}$ = 38.8 (c = 0.5, $CHCl_3$), The ee value was 91% [Chiralpak IA-3, hexane/i-PrOH = 90:10, 210nm, 1.0 mL/min, Major-anti-(t_{major} =22.83 min., t_{minor} =19.13 min), Minor-syn-(t_{major} =37.92 min., t_{minor} = 15.12 min)]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.58 – 7.48 (m, 2H), 7.43 – 7.32 (m, 5H), 7.00 – 6.89 (m, 2H), 5.72 (t, *J* = 13.3 Hz, 2H), 4.79 (br, 1H), 3.85 (s, 3H), 1.30 (s, 9H). Analytical and spectral data were in agreement with the literature data.[8]

Tert-butyl [(1S,2R)-2-(naphthalen-2-yl)-2-nitro-1-phenylethyl]carbamate (6ag)

White solid, 39.1 mg, 99% yield, dr=98:2, m.p. =183-186 ℃, $[a]_D^{20}$ = 45.6 (c = 0.5, $CHCl_3$), The ee value was 96% [Chiralpak IA-3, hexane/i-PrOH = 90:10, 210 nm, 1.0 mL/min, Major-anti-(t_{major} =30.77 min., t_{minor} =25.86 min),Minor-syn-(t_{major} =35.52 min., t_{minor} =14.65 min)]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.03 (s, 1H), 7.93 – 7.81 (m, 3H), 7.69 (d, *J* = 8.5 Hz, 1H), 7.59 – 7.48 (m, 2H), 7.44 – 7.33 (m, 5H), 5.97 (d, *J* = 9.9 Hz, 1H), 5.78 (br, 1H), 4.80 (d, *J* = 8.5 Hz, 1H), 1.16 (s, 9H). Analytical and spectral data were in agreement with the literature data.[8]

Tert-butyl [(1S,2R)-2-(2-fluorophenyl)-1-(4-methoxyphenyl)-2-nitroethyl]carbamate (6jb)

White solid, 38.5 mg, 98% yield, dr=99:1, m.p. =145-146 ℃, $[a]_D^{20}$ = 72 (c = 0.35, $CHCl_3$), The ee value was 98% [Chiralpak IA-3, hexane/i-PrOH = 10:1, 210 nm, 1.0 mL/min, Major-anti-(t_{major} =18.52 min., t_{minor} =16.50 min)]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (t, *J* = 7.3 Hz, 1H), 7.46 – 7.36 (m, 1H), 7.30 (t, *J* = 7.9 Hz, 1H), 7.23 (d, *J* = 7.7 Hz, 1H), 7.16 – 7.09 (m, 1H), 6.95 (d, *J* = 7.6 Hz, 1H), 6.88 (d, *J* = 8.3 Hz, 2H), 6.19 (d, *J* = 10.3 Hz, 1H), 5.70 (br, 1H), 4.82 (br, 1H), 3.81 (s, 3H), 1.23 (s, 9H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -117.8. Analytical and spectral data were in agreement with the literature data.[8]

Tert-butyl [(1S,2R)-2-(4-bromophenyl)-1-(4-methoxyphenyl)-2-nitroethyl]carbamate (6jd)

White solid, 45.1 mg, 99% yield, dr=97:3, m.p. =181-182 ℃, $[a]_D^{20}$ = 37 (c = 0.6, $CHCl_3$), The ee value was 96% [Chiralpak IA-3, hexane/i-PrOH = 80:20, 254 nm, 1.0 mL/min, Major-anti-(t_{major} =9.68 min., t_{minor} =36.58 min),Minor-syn-(t_{major} =26.66 min., t_{minor} =10.57 min)]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, *J* = 8.3 Hz, 2H), 7.46 (d, *J* = 8.3 Hz, 2H), 7.30 (d, *J* = 7.8 Hz, 1H), 6.89 (dd, *J* = 12.5, 7.8 Hz, 3H), 5.74 (d, *J* = 9.6 Hz, 1H), 5.61 (br, 1H), 4.76 (d, *J* = 9.4 Hz, 1H), 3.80 (s, 3H), 1.27 (s, 9H). Analytical and spectral data were in agreement with the literature data.[8]

Tert-butyl [(1S,2R)-1,2-bis(4-bromophenyl)-2-nitroethyl]carbamate (6hd)

White solid, 50 mg, 99% yield, dr=97:3, m.p. =183-185 ℃, $[a]_D^{20}$ = -13.2 (c = 0.5, $CHCl_3$), The ee value was 99% [Chiralpak IA-3, hexane/EtOH = 90:5, 230 nm, 1.0 mL/min, Major-anti-(t_{major} =23.64 min., t_{minor} =15.92 min), Minor-syn-(t_{major} =69.55 min., t_{minor} =29.89 min)]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.63 – 7.53 (m, 2H), 7.53 – 7.47 (m, 2H), 7.43 (d, *J* = 8.6 Hz, 2H), 7.22 (d, *J* = 8.4 Hz, 2H), 5.74 (d, *J* = 9.5 Hz, 1H), 5.56 (t, *J* = 9.6 Hz, 1H), 4.82 (br, 1H), 1.28 (s, 9H). Analytical and spectral data were in agreement with the literature data.[7]

Tert-butyl [(1R,2S)-1-nitro-1,4-diphenylbutan-2-yl]carbamate (6oa)

White solid, 34 mg, 91% yield, dr=94:6, m.p. =133-134 ℃, $[a]_D^{20}$ = 10.4 (c = 0.5, $CHCl_3$), The ee value was 97% [Chiralpak AD-H, hexane/i-PrOH = 95:5, 210 nm, 1.0 mL/min, Major-anti-(t_{major} =26.57 min., t_{minor} =38.17 min), Minor-syn-(t_{major} =33.70 min., t_{minor} =42.41 min)]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46 – 7.34 (m, 5H), 7.30 (d, *J* = 6.8 Hz, 1H), 7.21 (d, *J* = 6.9 Hz, 1H), 7.14 (d, *J* = 6.8 Hz, 2H), 5.65 (s, 1H), 4.55 – 4.27 (m, 2H), 2.89 – 2.74 (m, 1H), 2.72 – 2.56 (m, 1H), 1.94 (br, 2H), 1.33 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.0, 140.7, 132.2, 129.9, 128.9, 128.7, 128.5, 128.4, 126.3, 93.7, 80.1, 53.3, 32.8, 32.3, 28.3. HRMS (ESI): calculated for $C_{21}H_{26}N_2O_4Na^+$ ($[M+Na]^+$) 393.1785. Found 393.1777. Absolute and relative configurations were assigned on the analogy of **6aa.**

Derivatization of 6aa and 6ea

To a solution of **6aa** (34.2 mg, 0.10 mmol) in anhydrous MeOH (0.5 mL) was added $NiCl_2{\cdot}6H_2O$ (23.8 mg, 0.10 mmol) at room temperature. The mixture solution was cooled to 0 ℃ before $NaBH_4$ (56.7 mg, 1.50 mmol) was added in portions. The reaction mixture was then stirred for 2 h and poured into a saturated aqueous solution of NH_4Cl. The aqueous phase was extracted with ethyl acetate (5 mL) twice. The combined organic phases were washed with brine and dried over Na_2SO_4 and filtered. After concentration, the resulting residue was purified by column chromatography on silica gel (PE/EA=2:1 as eluent) to give 7**aa**.

To a solution of 7**aa** (31.2 mg, 0.10 mmol) in anhydrous CH_2Cl_2 (0.15 mL) was added trifluoroacetic acid (0.15 mL) at 0 ℃. The reaction mixture was then stirred for 2 h and poured into an ice-cooled 1 N aqueous solution of NaOH. The aqueous phase was extracted with CH_2Cl_2 (5 mL) twice. The com-

bined organic phases were washed with brine and dried over $MgSO_4$ and filtered. After concentration, the resulting residue was purified by column chromatography on silica gel (PE/EA=1:2 as eluent) to give **8aa**.

Determination of the ee value of ***8ea***

To a solution of **8ea** (5 mg, 1 equiv) in anhydrous CH_2Cl_2 (1 mL) was added Et_3N (6 μL, 2 equiv) and *m*-toluoylchloride (3 μL, 1.1 equiv) at rt. The reaction mixture was then stirred for 20 min and poured into a saturated aqueous solution of NH_4Cl. Take the organic phase 100 μL. After concentration, dissolved in 1 mL of isopropanol, determination by HPLC.

Tert-butyl [(1S,2R)-2-amino-1,2-diphenylethyl]carbamate (7aa)

White solid, 25.6 mg, 82% yield, dr=99:1, $[a]_D^{20}$ = 67 (c = 0.35, $CHCl_3$), The ee value was 99% [Chiralpak AD-H, hexane/i-PrOH = 97:3, 210 nm, 1.0 mL/min, Major-anti-(t_{major} =10.44 min., t_{minor} = 11.58 min).

^{1}H NMR (300 MHz, DMSO-d_6) δ 7.46 – 7.06 (m, 12H), 4.54 (t, *J* = 8.8 Hz, 1H), 3.97 (d, *J* = 8.4 Hz, 1H), 1.60 (br, 2H), 1.18 (s, 9H). ^{13}C NMR (101 MHz, DMSO-d6) δ 154.5, 143.9, 141.4, 127.8, 127.6, 127.5, 126.8, 126.5, 99.5, 77.5, 60.8, 59.6, 28.1. HRMS (ESI): calculated for $C_{19}H_{25}N_2O_2$ $[M+H]^+$: 313.1911, found 313.1903.

Tert-butyl [(1S,2R)-2-amino-1-(3-chlorophenyl)-2 phenylethyl]carbamate (7ea)

White solid, 26 mg, 75% yield, dr=98:2, $[a]_D^{20}$ = -17 (c = 0.2, $CHCl_3$), The ee value was 98% [Chiralpak IA-3, hexane/i-PrOH = 90:10, 210 nm, 0.5 mL/min, Major-anti-(t_{major} =20.39 min., t_{minor} = 22.88 min). ^{1}H NMR (300 MHz, CD_3OD) δ 7.43 – 7.19 (m, 9H), 4.85 (br, 1H), 4.79 (d, *J* = 7.8 Hz, 1H), 4.11 (d, *J* = 8.7 Hz, 1H), 1.27 (s, 9H). ^{13}C NMR (75 MHz, CD_3OD) δ 157.1, 144.0, 142.3, 135.4, 131.0, 129.4, 129.1, 128.9, 128.8, 128.7, 127.2, 80.4, 61.5, 61.0, 28.6. HRMS (ESI): calculated for $C_{19}H_{24}ClN_2O_2$ $[M+H]^+$: 347.1521, found 347.1521.

(1R,2S)-1,2-diphenylethane-1,2-diamine (8aa)

White solid, 19.3 mg, 97% yield, ^{1}H NMR (300 MHz, CDCl3) δ 7.34 – 7.16 (m, 10H), 4.10 (s, 2H), 1.55 (s, 4H). ^{13}C NMR (101 MHz, CDCl3) δ 143.5, 128.2, 127.0, 126.9, 61.9. HRMS (ESI): calculated for $C_{14}H_{17}N_2$ $[M+H]^+$: 213.1386, found 213.1380.

(1S,2R)-1-(3-chlorophenyl)-2-phenylethane-1,2-diamine (8ea)

White solid, 22.9 mg, 94% yield, $[a]_D^{20}$ = 89 (c = 0.5, $CHCl_3$), The ee value was 98% [Chiralpak IC-3, hexane/i-PrOH/EtOH = 80:14:6, 254 nm, 0.5 mL/min, Major-anti-(t_{major} =12.21 min., t_{minor} = 12.76 min).^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.57 – 7.00 (m, 9H), 4.12 – 3.89 (m, 2H), 1.51 (br, 4H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.3, 142.6, 134.5, 129.7, 128.6, 127.9, 127.6, 127.7, 127.65, 126.1, 62.8, 62.5. HRMS (ESI): calculated for $C_{14}H_{16}ClN_2$ $[M+H]^+$: 247.0997, found 247.1002.

ASSOCIATED CONTENT

Supporting Information

Detailed experimental procedures including complete characterizations (^{1}H NMR and ^{13}C NMR spectra, spectral data, and HRMS).This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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